AMENDMENTS TO THE TITLE:

Please amend the title wherever it appears as follows:

HBV DRUG RESISTANCE ~~DRUG RESISTANCE DETECTION~~ METHODS

AMENDMENTS TO THE SPECIFICATION:

Amend the specification as follows:

Please amend the Title on line 1 of page 1 as follows:

HBV DRUG RESISTANCE ~~DETECTION~~ METHODS

Please amend the paragraph spanning lines 6-17 of page 14 of the specification as follows:

Modifications of nucleotides include the addition of acridine or derivatives thereof, ACRYDITE[[Acrydite™]], amine, biotin, BHQ-1, BHQ-2, BHQ-3~~BHQ-1™, BHQ-2™, BHQ-3™~~, borane dNTPs, carbon spacers (e.g. C_3, C_6, C_7, C_9, C_{12} or C_{18}), cascade blue, cholesterol, coumarin or derivatives thereof, Cy3, Cy3.5, Cy5, Cy5.5, Cy7~~Cy3®, Cy3.5®, Cy5®, Cy5.5®, Cy7®~~ DABCYL, dansylchloride, digoxigenin, dinitrophenyl, dual biotin, EDANS, 6-FAM, fluorescein, 3'-glyceryl, HEX, IAEDANS, inverted dA, inverted dG, inverted dC, inverted dG, IRD-700, IRD-800, JOE, La Jolla Blue, metal clusters such as gold nanoparticles, phenylboronic acid, phosphate psoralen, 3'- or 5'-phosphorylation, pyrene, 3' ribo-adenosine, 3' ribo-guanosine, 3' ribo-cytidine, (LC)Red640, (LC)Red705, rhodamine, ROX, thiol (SH), spacers, TAMRA, TET, AMCA-S, SE, BODIPY, MARINA BLUE, OREGON GREEN, PACIFIC BLUE, QSY7, RHODAMINE GREEN, RHODAMINE RED, RHODOL GREEN, tetramethylrhodamine, TEXAS RED ~~AMCA-S®, SE, BODIPY®, Marina Blue®, Oregon Green®, Pacific Blue®, QSY7™, Rhodamine Green®, Rhodamine Red®, Rhodol Green®, tetramethylrhodamine, Texas Red®~~, Uni-Link NH_2-modifier, radiolabels (e.g. ^{125}I, ^{131}I, ^{35}S, ^{14}C, ^{32}P, ^{33}P, ^{3}H) and nanoparticles.

Please amend the paragraph spanning lines 1-16 of page 28 of the specification as follows:

A hairpin primer comprising a Molecular Beacon-type structure, its loop, however, not binding to the target DNA and further comprising a 3' single stranded extension capable of hybridizing to the target DNA can be used for direct detection of the PCR amplified target DNA. Said amplification can be followed by measuring the increasing fluorescence as the hairpin is present in the amplicon in an open conformation. This hairpin primer-type is known as SUNRISE[[Sunrise™]] primers. Such hairpin primers can also be designed in the allele-specific format and can as well be used to prime rolling circle amplification of circularized padlock primers in conjunction with a second primer capable of priming complementary strand DNA synthesis (Faruqi et al., 2001; Nazarenko et al., 1997). Rolling circle amplification is explained in more detail *infra*. Another variation on the same theme is the one wherein the initial PCR cycle is primed with allele-specific primers comprising a 'universal' 5'-tail capable of hybridizing with a 'universal' tailed Sunrise-type probe. These 'universal', tailed hairpin primers are known as AMPLIFLUOR[[Amplifluor™]] primers. Starting from the third cycle these Amplifluor primers act in priming DNA synthesis and starting from the fourth cycle synthesis of the strand complementary to the Amplifluor primer-primed ssDNA results in opening of the hairpin and, thus, the appearance of fluorescence (Myakishev et al., 2001).

Please amend the paragraph spanning lines 4-14 of page 33 of the specification as follows:

Base excision sequence scanning (BESS) is a technique involving incorporation of dUTP in an amplified target DNA molecule. Said target molecule is subsequently digested in the BESS-T[[TM]]-Scan reaction (Epicentre Technologies, Madison, WI, USA) with an enzyme mix comprising uracil-N-glycosylase (UNG) and *E. coli* endonuclease IV. The action of both enzymes result in a cleavage of the DNA at the site of dUTP incorporation. In the BESS-G-TRACKER[[Tracker™]] reaction (Epicentre Technologies, Madison, WI, USA), deoxyguanosines are modified followed by enzymatic excision of the modified deoxyguanosines and cleavage of the DNA. Separation by gel electrophoresis of both reaction products results in T and G ladders analogous to those obtained via dideoxysequencing (see *infra*). Comparison with a reference DNA analyzed the same way allows identification of nucleotide sequences polymorphisms (Hawkins et al., 1999).

Please amend the paragraph spanning lines 26 of page 33 through line 4 of page 34 of the specification as follows:

Cycle sequencing is based on the Sanger reaction but a thermostable polymerase is utilized. Contrary to PCR, a single primer is used in cycle sequencing. Due to the linear amplification of the target DNA, far less template DNA is required for cycle sequencing as compared to classical dideoxysequencing. Furthermore, the need to prepare single-stranded sequencing template is eliminated. ddNTPs can each be labeled with a different fluorescent tag ('dye terminators') allowing analysis of four

reactions/dyes in a single gel lane. Alternatively, the label can be incorporated in the primer ('dye primers'). PCR (or RT-PCR) and sequencing can also be coupled in a single reaction, known as CAS (coupled amplification and sequencing), or a modification thereof known as CLIP[[TM]] which is run on the Visible Genetics Clipper sequencer which uses MICROCEL[[MicroCel™]] polyacrylamide gel cassettes. CLIP[[TM]] Sequencing enables single-tube, simultaneous determination of the nucleotide sequence from both directions of a PCR amplicon using two sequencing primers labeled with a different dye (Cy5 and Cy5.5). (Yager et al., 1999; Ruano et al., 1991).

Please amend the paragraph spanning lines 25-29 of page 35 of the specification as follows:

Alternatively, ACRYDITE[[Acrydite™]]-modified oligonucleotide probes are copolymerized into a polyacrylamide gel. Single-stranded target DNA targets are electrophoresed through said gel and, depending on electrophoresis conditions (temperature and/or denaturant), captured by the oligonucleotides immobilized in a capture gel layer. This method is also applicable for detecting nucleotide sequence polymorphisms (Kenney et al., 1998).

Please amend the paragraphs spanning lines 28-31 of page 36 of the specification as follows:

Commonly used fluorescent dyes include BODIPY FL, CY3, CY3.5, CY5, CY5.5~~Cy3®, Cy3.5®,Cy5®, Cy5.5®~~, EDANS, FAM, fluorescein, HEX, IAEDANS, JOE,

[[Oregon Green®]] ORANGE GREEN, (LC)Red640, (LC)Red705, ROX, TAMRA, TET, tetramethylrhodamine and [[Texas Red®]] TEXAS RED.

Commonly used quencher dyes include BHQ-1[[TM]], BHQ-2[[TM]], BHQ-3[[TM]], DABCYL, metal clusters such as gold nanoparticles (Dubertret et al., 2001) and QSY7[[TM]].